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Comparison of healing of the osteotomy gap after tibial tuberosity advancement with and without use of autogenous cancellous bone graft

Inaugural-Dissertation

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1 Summary

Healing of the gap created during Tibial Tuberosity Advancement (TTA) with and without the use of bone graft was evaluated in 28 (prospective study) and 39 (case series) cases in this prospective study and case series.

Medio-lateral radiographs, taken 6 weeks and 4 months postoperatively, of 14 TTAs operated without the use of bone graft (group I) were compared with radiographs of 14 consecutive cases with comparable osteotomies, in which the gaps were filled with autologous cancellous bone graft (group II). Two radiologists evaluated the follow-up radiographs independently, unaware of the procedure details, using two different scoring techniques (A and B). Score A was used to grade healing of the osteotomy site, using a 0-4 scale. Score B was used to evaluate, independently of each other, bone healing in three areas: proximal to the cage (B1), between cage and plate (B2), and distal to the plate (B3).

Medio-lateral radiographs of 39 dogs after TTA without grafting the gap were evaluated for healing using score A for the case series.

Score A showed no statistical difference in healing between groups at each time in the prospective study. Score B1 revealed, in both radiographic controls, a significant higher density of bone healing in the group II than in group I. Scores B2 and B3 showed not significantly different between groups. Healing occurred in all cases at similar times reported in previous studies in the case series.

The osteotomy gap created during TTA healed regardless of using or not using bone graft. Without bone graft operative time, morbidity, and /or costs are reduced.

2 Introduction

Tibial Tuberosity Advancement (TTA) was developed at the University of Zurich in 2002, to restore dynamic stability in cranial cruciate ligament-deficient (CrCLD) stifles in dogs.[1,2] Stability is accomplished by an osteotomy of the tibial tuberosity in the frontal plane with advancement of the insertion of the patellar ligament.[1,2] By changing the angle between patellar tendon and tibial plateau to 90° during the stance phase of the gait, shear forces are eliminated and the stifle renders dynamically stable.[2] *In vitro* experimental studies validated the mechanics of TTA,[3-6] and clinical reports showed a satisfactory function after surgery. [7-9]

Using the commercially available implants (Kyon; Zurich, Switzerland), and performing the technique as previously described,[7-11] a proximal bone gap from 3 to 12 mm width area is created.

As initially described, the opening wedge osteotomy was filled with autogenous cancellous bone graft taken from the body of the tibia, caudal to the osteotomy.[1,9-11] Other reported options are to harvest the graft from the distal femur,[7,8] to use allograft,[7] xenograft,[12] to position a block of tricalcium phosphate,[1] or to fill the defect with nanohydroxyapatite (Owen MO. Experiences with use of nanohydroxyapatite paste to augment cancellous bone autografting in the TTA procedure. KYON 2008 Symposium: Innovations in Veterinary Orthopaedics and Trauma. Zurich, Switzerland; April 19, 2008).

The use of autogenous cancellous bone graft increases operative time and morbidity.[13-21] Adding commercially available allograft is convenient,[7] but increases the costs in about US Dollars 200 per patient.[17] Nanohydroxyapatite paste (Ostium®; Heraeus Kulzer Inc., Armonk, NY) increases costs in about 100 US Dollars per dog.[17]

Based on literature data, healing seems to occur regardless of the grafting material used.[7-9] The osteotomy gap is created in the richly vascularised metaphysis. We therefore hypothesize that healing of the gap created during TTA will occur in absence of any grafting material.

This study was divided in two parts. The purpose of the first part was to radiologically evaluate and compare healing of the osteotomy gap with and without the use of fresh autogenous cancellous bone graft taken from the proximal tibia. Our null hypothesis was that radiographically determined healing would not differ between grafted and non-grafted TTAs. In the second part of the study, healing in a larger group of dogs was evaluated. Here we hypothesized that no difference in healing time would be observed between our group and the healing times observed in other studies.

3 Material and Methods

This project was divided into a pilot study used to test our null hypothesis, and a second part in which all the dog operated after conclusion of the pilot study with at least one radiographic control were evaluated. All owners signed a consent form allowing all documentation regarding their dogs to be used for scientific research and publication.

The pilot study was composed by 14 TTAs performed in 14 client-owned dogs of 6 different large breeds (Table 1), in which TTA was performed without harvesting bone graft from the proximal tibia, and without filling the opening gap with any grafting material (group I). The osteotomy was performed with an oscillating saw. The osteotomy gap remained undisturbed during surgery without flushing and suctioning in group I. All dogs were skeletally mature and diagnosed as having a complete or partial CrCL rupture. Data retrieved from medical records included breed, body weight, gender, cage sizes and time of radiographic examinations. Medio-lateral follow up radiographs taken at approximately 6 weeks and 4 months postoperatively were evaluated.

A control study was composed of 14 TTAs performed in 11 client-owned dogs of 8 different large breeds (Table 1) that were grafted with autogenous cancellous bone graft obtained from the body of the tibia, caudal to the osteotomy (group II).

Table 1: Breed distribution in group I and II

	Group I	Group II
Breed	mixbreed dog (5) Golden Retriever (3) Bernese Mountain dog (2) Dalmatian (2) Dogue de Bordeaux (1) Belgian Shepherd dog (1)	mixbreed dog (6) Hovawart (2) German Boxer (1) German Shepherd dog (1) Labrador Retriever (1) Cocker Spaniel (1) St. Bernard (1) Golden Retriever (1)

Two radiologists evaluated progression of healing independently, unaware of the procedure details, using two different scoring techniques (A and B). Score A taken from a previous study,[8] uses 5 possible evaluations: 0 no bone healing, 1 early bone production without bridging between the tibial tuberosity and the shaft of the tibia, 2 bridging bone formation at one site, 3 indicating bridging bone at two sites, and 4 representing bridging bone at all three areas (Table 2). The sites were defined as the region of osteotomy proximal to the cage, between the cage and the plate, and distal to the plate (Figure 1).

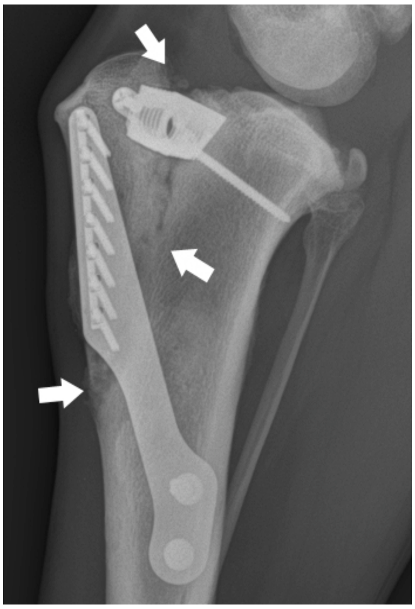


Figure 1: Six weeks follow-up radiograph of a non-grafted TTA. Score A evaluates healing of the osteotomy at the areas proximal to the cage, between plate and cage, and distal to the cage (arrows). Follow-up radiographs were taken at approximately 6 weeks and 4 months postoperatively. Score 0 means no bone healing in any area, 1 means early bone production without bridging between the tibial tuberosity and the shaft of the tibia, 2 means bridging bone formation at one site, 3 indicates bridging bone at two sites, and 4 represents bridging bone at all three areas.

The B score evaluated, independently of each other, bone healing in the same three areas; B1 scores the region proximal to the cage, B2 scores the region between the cage and the plate, and B3 scores the anatomic region distal to the plate. A 0 to 3 scale was used in each region, 0 means no callus noted, 1 means density of callus less than normal, 2 means density of callus equalling density of original bone, and 3 means density of callus exceeding original bone (Table 2). Original bone density was defined as bone density in the tibial shaft approximately 1 cm caudal to the osteotomy site (Figure 2).

Table 2: Evaluation Scores

	0	1	2	3	4
Score A	No bone healing	Early bone production without bridging between the tibial tuberosity and the shaft of the tibia	Bridging bone formation at one site	Bridging bone at two sites	Bridging bone at all three sites
Score B1	No osseous healing	Density is less than original bone	Like original bone	Higher than original bone	
Score B2	No osseous healing	Density is less than original bone	Like original bone	Higher than original bone	
Score B3	No osseous healing	Density is less than original bone	Like original bone	Higher than original bone	

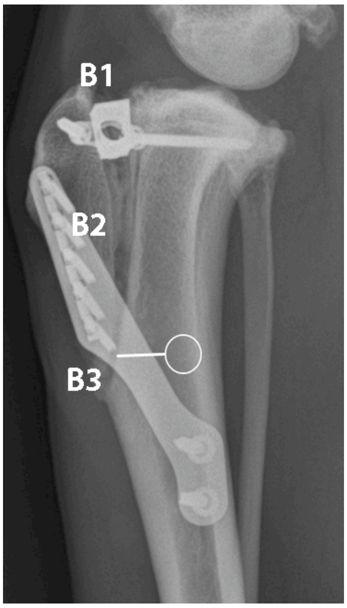


Figure 2: Six weeks follow-up radiograph of a non-grafted TTA. Score B evaluated, independently of each other, bone density in the same three areas, reflecting B1 the region proximal to the cage, B2 the region between the cage and the plate, and B3 the anatomic region distal to the plate. Follow-up radiographs were taken at approximately 6 weeks and 4 months postoperatively. A 0-3 scale was used in each region, meaning 0 no osseous healing, 1 density of callus less than normal, 2 density of callus equalling density of original bone, and 3 density of callus higher than original bone. Original bone density was defined as bone density in the tibial shaft approximately 1 cm caudal to the osteotomy site (circle with a 1 cm scale).

The second part of the study was composed of all dogs in which TTA was performed without grafting the gap after completion of the pilot study (December 2007- January 2009), and that had at least one radiographic study controlled for healing. Two radiologists independently and unaware of the time interval after surgery evaluated the radiographs using score A. Owners of dogs that did not perform any radiographic control at our institution were telephonically reached to ensure absence of clinical complications, but those cases were not included. Data retrieved from medical records included breed, body weight, gender, cage sizes, and time of radiographic examination.

Statistical Analysis

In the pilot study, groups were compared using unpaired t-tests, and factorial analysis of variance (ANOVA) was used.

To evaluate the results in the second part of the study an absolute risk score was made with a residual analysis to assess healing in course of the time, and to correlate healing with age, body weight, and cage size.

Data were analyzed using statistical software (StatView 5.1, SAS Institute Inc, Wangen bei Dübendorf, Switzerland). Statistical significance was set at $P \leq 0.05$. Results are present as mean ± standard deviation (SD).

4 Results

Follow-up radiographs, taken approximately six weeks and four months postoperatively, of 14 consecutive dogs receiving TTA in which the opening gap was not filled with autologous cancellous bone graft (group I) were compared to radiographs of 14 TTAs in which the gap was filled with bone graft taken from the proximal tibia, caudal to the osteotomy (group II).

Group I comprised 14 large dog breeds with a body weight of 30.571 ± 14.51 kg. Age was 5.214 ± 2.60 years. They were 9 females (7 neutered) and 5 males (3 castrated). Cage size ranged between 3 and 9 mm (6.214 ±1.178). Breeds represented in the group I were (n = stifles) mixbreed (5), Golden Retriever (3), Bernese Mountain dog (2), Dalmatian (2), Dogue de Bordeaux (1), Belgian Shepherd dog (1) (Table 1). Mean ± SD first radiographic control was performed at 6.86 ± 1.187 weeks. The second control took place at 4.29 ± 0.452 months (Table 3).

Table 3: Time (in weeks (1st control) and months (2nd control)) of performed follow-up radiographs in group I and II and statistical significance

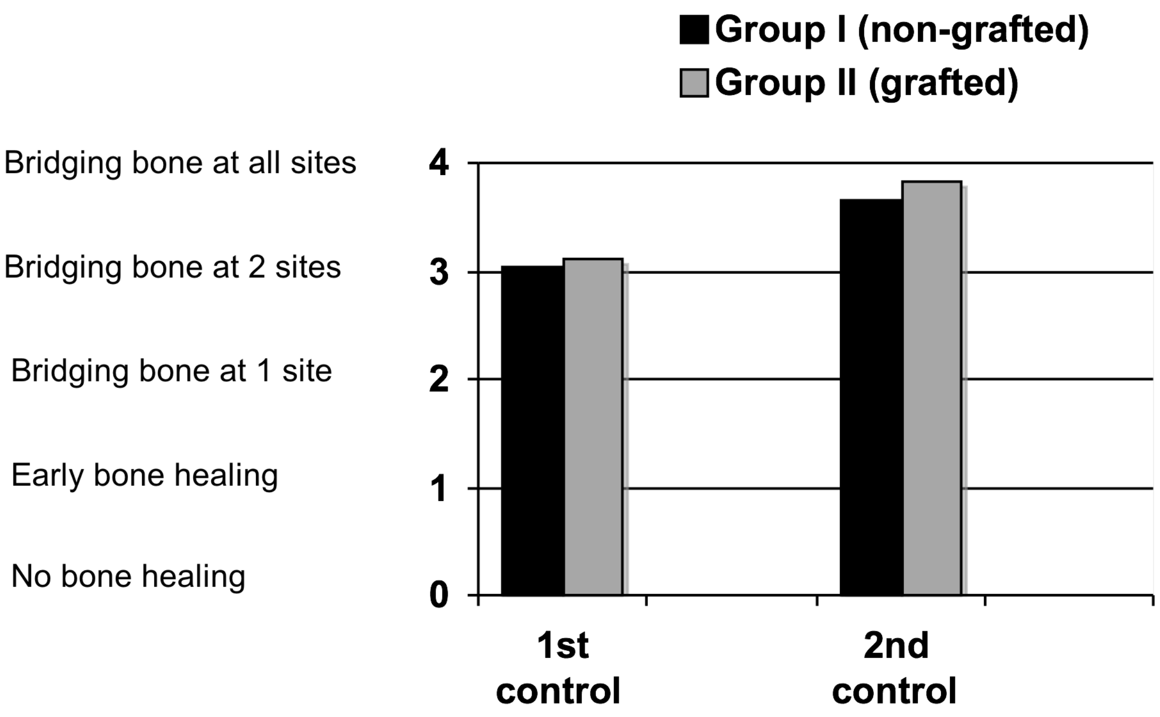
Follow-up	Group I	Group II	p-Value
1st control	6.86±1.187	6.79±1.145	0.383
2nd control	4.29±0.452	4.21±0.558	0.459

Group II comprised 14 TTAs performed in 11 large breed dogs in which the gap was filled with cancellous bone graft taken from the proximal tibia. Body weight was 33.607 ± 6.72 kg, age was 5.857 ± 2.59 years. There were 7 females (4 neutered) receiving 9 TTAs and 4 males castrated receiving 5 TTAs. Cage size ranged between 3 and 9 mm (7.5± 1.5). Breeds represented in the group II were mixbreed (6), Hovawart (2), Boxer (1), German Shepherd dog (1), Labrador Retriever (1), Cocker Spaniel (1), Saint Bernard (1), Golden Retriever (1) (Table 1). Radiographic controls were performed at 6.79 ± 1.145 weeks and at 4.21 ± 0.558 months (Table 3). No significant difference was found in age, body weight, size of cage, and time of radiographic controls between groups. Score A was, at the first radiographic control, 3.036 ± 0.571 for group I, and 3.107 ± 0.764 for group II. At the second radiographic control score A was 3.643 ± 0.535 for group I, and 3.821 ± 0.372 for group II (Table 4, Figure 3). There was no statistically significant difference for score A between group I and group II in any of the controls. A statistically significant difference between first and second follow-up control was found comparing healing scores.

Table 4: Comparison of the means of group I and II for score A, 6 weeks and 4 months after surgery and statistically significance

Time	Group I	Group II	p-Value
6 weeks	3.036±0.571	3.107±0.764	0.44
4 months	3.643±0.535	3.821±0.372	0.62

Figure 3: Chart illustrating the results of score A at the first and second radiographic control. No difference in healing is observed at both controls. Healing progressed significantly between controls.



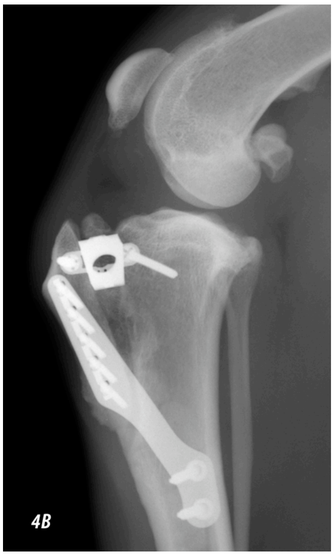
Score B1 (area proximal to the cage) at 6 weeks follow-up, was 0.83 ± 0.601 for group I, and 1.80 ± 0.82 for group II. At the second radiographic control it was 1.44 ± 0.73 for group I, and 2.05 ± 0.61 for group II. The difference was statistically significant between groups at each time interval (Table 5, Figure 4 A and B, Figure 6 A and B)

Table 5: Comparison of the means of group I and II for Score B1-B3, 6 weeks and 4 months after surgery and statistical significance

Score	Time	Group I	Group II	p-Value
B1	6 weeks	0.83±0.6	1.80±0.82	0.0015
B1	4 months	1.44±0.73	2.05±0.61	0.0247
B2	6 weeks	1.50±0.49	1.36±0.39	0.4
B2	4 months	1.93±0.65	1.64±0.27	0.14
B3	6 weeks	1.46±0.52	1.07±0.51	0.066
B3	4 months	2.00±0.48	1.86±0.65	0.514

Figures 4 A and 4 B: First radiographic control, approximately 6 weeks postoperatively, of a dog of group I (Figure 4 A) and of group II (Figure 4 B). Less healing is observed in the area proximal to the cage in the non-grafted dog.

4 A

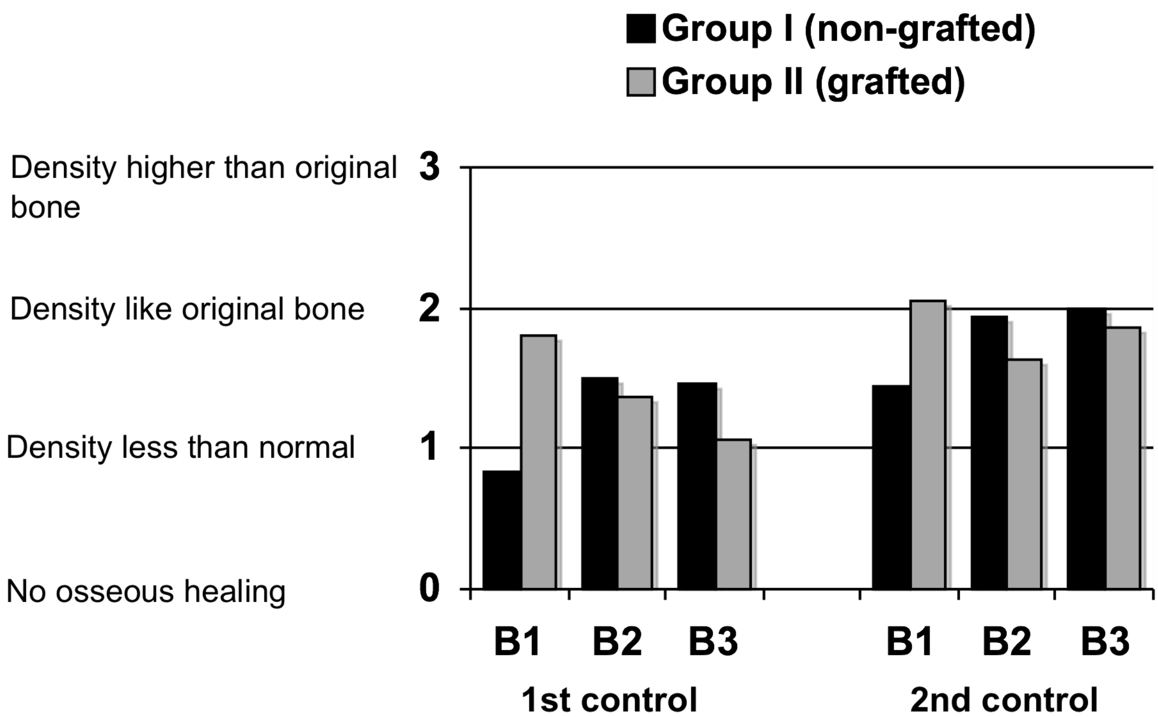


4 B

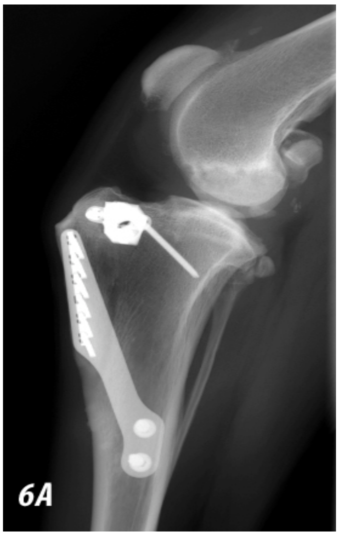
Score B2 during the first control was 1.50 ± 0.49 for group I, and 1.36 ± 0.39 for group II. At the second control group I scored 1.93 ±0.65, and group II scored 1.64 ± 0.27. Score B3 at the first control was 1.46 ± 0.52 for group I, and 1.07 ± 0.51 for group II, and at the second control 2.00 ± 0.48 for group I and 1.86 ± 0.65 for group II.

In the areas B2 and B3 were no statistically significant differences noted between groups at each control. In both groups osseus density of the gap increased at all 3 sites between first and second follow-up examination (p-value 0.0467) (Figure 4 A and 4 B, Figure 5 and Figure 6 A and 6 B).

Figure 5: Chart illustrating the results of score B at 6 weeks and 4 months radiographic control. The area B1 showed statistically significant differences between groups at each control. No differences were observed between the other groups. Healing progressed significantly between time intervals.



Figures 6 A and 6 B: 4 months radiographs of a non-grafted dog (A) and a grafted dog (B). Score A showed no differences in healing between groups. Score B showed, except from the area proximal to the cage, no differences in healing.

6 A 

6 B 

Thirty-nine dogs (20 spayed females, 13 castrated males, and 6 intact males) with a body weight of 29.2 ± 11.6 (range 7.3-62 kg), and an age of 5.9 ± 2.97 years (range 1-12 years) meet the inclusion criteria for the second part of the study. Cage size ranged between 3 and 12 mm (mean ± SD 7 ± 1.96). The group comprised: mixbreed dog (9), Labrador Retriever (3), Rottweiler (2), Border Collie (2), Beagle (2), German Boxer (2), Continental Bulldog (2), White Swiss Shepherd dog (1), Australian Shepherd dog (1), Kangal (1), Maremmano (1), German Shepherd dog (1), Akita Inu (1), West Highland White Terrier (1), Jack Russell Terrier (1), Dogue de Bordeaux (1), Flat Coated Retriever (1), Golden Retriever (1), Vizsla (1), American Staffordshire Terrier (1), American Bulldog (1), Bergamasco (1), Doberman Pinscher (1), and Laika dog (1) . Follow-up radiographs were taken at 11.59 ± 5.99 weeks after surgery (range 4-25 weeks). Mean healing score A was 3.4 (range, 2 – 4) and progressed significantly over time (Table 6). 89.7 % of the stifles scored 3 or 4 at control. Healing of the osteotomy gap was assessed as complete (grade 4) in 23 cases (58.9%) at recheck time. The mean follow up time for this group was 14.6 weeks (range 6-25 weeks). Twelve stifles (30.7%) scored 3, and 4 stifles (10.2%) scored 2. Radiographs of stifles scoring 3 were taken at a mean time of 8.16 weeks (range 6-15 weeks), and those of stifles scoring 2 were taken at 5 weeks (range 4-6 weeks). No healing-related complications were detected in any case. Healing of the gap proceeded in course of time statistically significant ($p<0.0001$). Healing in course of time was not depending on age, body weight, and/or size of the cage.

Table 6: Means of results of score A for the second part group and statistical significance of proceeding in gap healing in course of time

Score	Mean result	p-Value
A	3.4±0.67	<0.0001

5 Discussion

All of the TTA procedures performed with and without fresh autogenous cancellous bone graft had a satisfying outcome.

The osteotomy was performed with an oscillating saw. The osteotomy gap was left undisturbed during surgery without flushing and suctioning in non-grafted TTAs. We assume that the remaining blood clot in the gap with its pluripotential mesenchymal cells coming from the endosteal surface at the osteotomy site may enhance the bone healing due to its osteogenetic and osteoinductive properties.

Two scores were used to evaluate healing. Score A, taken from a previous study,[8] was used to compare healing of the osteotomy in the pilot study, and to compare healing of our case series with other published reports. Using this score, in the pilot study, we could not identify differences in healing between groups.

Score B, used in the pilot study to evaluate bone density in three different areas of the osteotomy gap separately, showed that except from the area proximal to the cage, the osteotomy gap healed at similar times regardless of using or not using bone graft. Bone graft was packed in this area in the grafted group and this may have enhanced healing in this area in which otherwise the retropatellar fat pad is present. The delayed healing in this area in non-grafted dogs apparently did not cause any clinical problem.

A limitation of the first part of the study is the small number of cases. Healing between two groups of 14 animals each was compared and this may be not enough to obtain conclusive results, but using a small group was justified to get early evaluation and not to expose too many patients to the risk of a non-union at the TTA site. Grafting TTAs was not longer performed at our institution based on the favorable results of the first part of this study. Subsequent cases were radiographically evaluated and scored using score A. Bone healing occurred progressively over time and at a similar rate as reported in previous studies. Complete healing was previously reported to occur at about 11 weeks.[7,8] One of these studies does not describe how healing was evaluated making comparison difficult.[7] Complete healing at a mean time of 14.6 weeks postoperatively was reported in this study, but because only one radiographic control was performed, the exact point of complete healing cannot be defined and is presumably at some point before this date. 9 of 23 cases (39.1%) that were scored with 4 received the only radiographic control at more than 16 weeks. Eliminating these cases gave a mean time to complete healing of 11 weeks, which compares similarly with other reports.

Partial healing (scores 2 and 3) was observed at 5 and 8 weeks comparing similarly with a previous study.[8]

Nine mm cages are the most commonly used, and together with the 6 mm cages, represent about 95 % of the used sizes.[8] No 12 mm cages were used in the first part of this study, and only 3 in the second part of it. Apparently large advancements heal in the same way as the advancement created by 6 and 9 mm cages, but to obtain conclusive results, more cases using large size of cages may be needed.

The use of fresh autogenous cancellous bone graft increases surgical time,[15] and an additional surgical approach may be needed, increasing morbidity.[21] Other disadvantages of the use of fresh autogenous cancellous bone graft are disrupted blood supply, fracture at the donor site,[13,14,16,21] post-operative bleeding,[20,21] seroma formation,[14] and infection.[15]

In human beings a well-known sequela of harvesting autogenous bone graft is chronic pain that may last for more than 6 months.[18,19,] The cause of donor-site pain is believed to result from nerve injury or destabilization of the muscular origin at the time of harvest. [22,23] This has not be documented in animals, but additional surgical trauma and a separate approach to harvest bone graft from the distal femur[7,8,17]may cause haemarthrosis, unnecessary pain and discomfort.

Using commercially available allograft,[7,17] or another bone substitute[12] (Owen MO. Experiences with use of nanohydroxyapatite paste to augment cancellous bone autografting in the TTA procedure. KYON 2008 Symposium: Innovations in Veterinary Orthopaedics and Trauma. Zurich, Switzerland; April 19, 2008) are reported options to avoid harvesting autograft, but these options increase the surgical costs, making then unviable in many countries, and apparently are not necessary.

In conclusion and according to our results, the osteotomy gap created during TTA healed with or without bone graft at similar rates than reported in previous studies[7,8] making the use of bone graft unnecessary.

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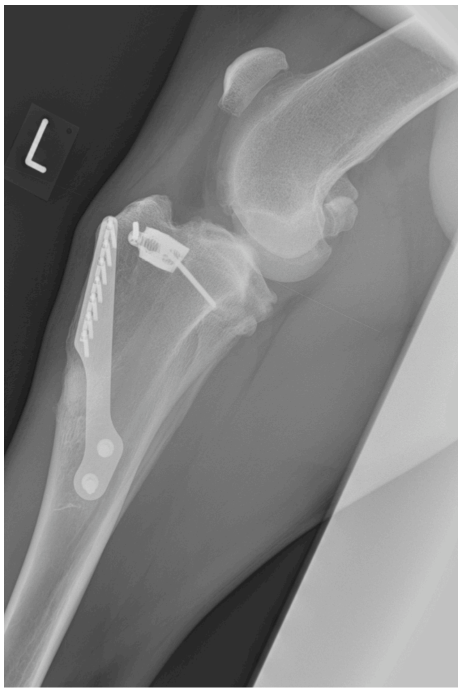
7 Appendix

Figure 7: Group I 1st(A1-E1) and 2nd(A2-E2) control

A1

A2

B1



B2

C1

C2

D1

D2

E1

E2

Figure 8: Group II 1st(A1-E1) and 2nd(A2-E2) control

A1

A2

B1

B2

C1

C2

D1

D2

E1

E2

Danksagung

Mein besonderer Dank geht an Prof. Dr. Pierre M. Montavon und Dr. Tomás Guerrero für die Überlassung des Themas, die gute Zusammenarbeit und die exzellente fachliche Betreuung.

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Lebenslauf

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